Management of children with travel-related illness evaluated in a pediatric emergency room

Leuthard, Deborah ; Berger, Christoph ; Staubli, Georg ; Nadal, David ; Schmid, Sabine ; Hamer, David ; Weber, Rainer ; Schlagenhauf, Patricia

Abstract: BACKGROUND: Children travelling are potentially exposed to a wide spectrum of illness, which includes mild self-limiting disease, but also severe illness requiring hospitalization. Risk factors for hospitalization need to be analysed to inform prevention- and treatment strategies for travel-related disease, to make travelling for children - from a medical perspective - more secure. METHODS: We performed a cross-sectional analysis on children with travel-related disease presenting at the Emergency Room of University of Zurich Children's Hospital between July 2007 and December 2012. The profile of children being hospitalized was compared to that of children treated as outpatients. RESULTS: 801 children (57.4% male) were included in the study. 83 children (10.4%) were treated as inpatients. Compared to outpatients, inpatients were significantly more likely to be male, to have travelled to Southern Asia, to have a diagnosis of Salmonella typhi or paratyphi(3.6 % vs. 0.1%, $p < 0.0001$), pyogenic abscess (3.6% vs. 0.1 %, $p < 0.0001$) or malaria (1.4 % vs. 0.2%, $p = 0.0384$). Neurologic diagnoses (such as seizure disorder: 3.6% vs. 0.4%, $p < 0.0001$) were diagnosed more often among inpatients. Furthermore, inpatients presented more often with non-specific findings such as dehydration (8.5% vs. 0.6%, $p < 0.0001$): No correlation with inpatient care was seen for VFR/immigrant travel. CONCLUSIONS: Children acquire a wide spectrum of travel-related illness. A careful, detailed travel history is important in children presenting in the Emergency Room with symptoms suggesting infectious disease.

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Management of Children with Travel-related Illness Evaluated in a Pediatric Emergency Room

Deborah Leuthard, MMed,†‡ Christoph Berger, MD,†‡ Georg Staubli, MD,†‡ David Nadal, MD,†‡ Sabine Schmid, MD,* David Hamer, MD,§¶‖ Rainer Weber, MD,** and Patricia Schlagenhauf, PhD**

Background: Children travelling are potentially exposed to a wide spectrum of illness, which includes not only mild self-limiting disease but also severe illness requiring hospitalization. Risk factors for hospitalization need to be analyzed to inform prevention and treatment strategies for travel-related disease, to make travelling for children—from a medical perspective—more secure.

Methods: We performed a cross-sectional analysis on children with travel-related disease presenting at the Emergency Room of University of Zurich Children's Hospital between July 2007 and December 2012. The profile of children being hospitalized was compared with that of children treated as outpatients.

Results: Eight hundred and one children (57.4% male) were included in the study. Eighty-three children (10.4%) were treated as inpatients. Compared with outpatients, inpatients were significantly more likely to be male, to have travelled to Southern Asia, to have a diagnosis of *Salmonella typhi* or *Salmonella paratyphi* (3.6 % vs. 0.1%, $P < 0.0001$), pyogenic abscess (3.6% vs. 0.1 %, $P < 0.0001$) or malaria (1.4 % vs. 0.2%, $P = 0.0384$). Neurologic diagnoses (such as seizure disorder: 3.6% vs. 0.4%, $P < 0.0001$) were diagnosed more often among inpatients. Furthermore, inpatients presented more often with nonspecific findings such as dehydration (8.5% vs. 0.6%, $P < 0.0001$). No correlation with inpatient care was seen for visiting friends and relatives/immigrant travel.

Conclusions: Children acquire a wide spectrum of travel-related illness. A careful, detailed travel history is important in children presenting in the emergency room with symptoms suggesting infectious disease.

Key Words: travel, children, infection, inpatient, outpatient

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International travel increased from 25 million international tourist arrivals in 1950 to 528 million in 1995; in 2013, worldwide travel reached a record of 1087 million arrivals. During the period 2010–2030, the number of international tourist arrivals worldwide is expected to increase by an average of 3.3% a year.[1] There are limited data on the proportion of children in international traveler statistics, but data from the US show that approximately 31% of adults travel with children.[2] In Switzerland, children aged between 6 and 14 years undertook on average 1.3 visits into another country in 2012. There were no data available for children younger than 6 years of age.[3] Zürich is an international city, and tourist, immigrant and visiting friends and relatives (VFR) travel are common. In 2010, 85.5% of the population undertook at least 1 private trip with overnight stays, of which 60% were trips to foreign countries.[4] Because of socioeconomic and demographic changes, Switzerland has become an ethnically diverse country, leading to increased immigrant and VFR travel; 26% of the children born in Switzerland in 2010 had a foreign citizenship.[4] A significant proportion of children travelling will develop travel-related illness.[5] In some cases, children may present with a severe and/or a rarely diagnosed infection. The diagnosis of such exotic infections often poses a challenge for the emergency room (ER) team, especially if the illness is severe. Being hospitalized because of a travel-related illness has significant impact on children and healthcare systems and may be avoidable by taking the necessary precautions. We aimed to evaluate which travel-related illnesses, risk factors, travel destinations and types of travel are associated with hospitalizations in children, by comparing pediatric inpatients and outpatients at Zürich University Children's hospital.

MATERIALS AND METHODS

Our study focused on children presenting to the University of Zürich Children's Hospital. We performed a cross-sectional analysis and compared children with travel-related disease who were hospitalized with those who were treated as outpatients. The University of Zurich Children's Hospital, as part of the GeoSentinel[6] surveillance network (www.geosentinel.org), provides clinician-based pediatric data for this study. Data were prospectively collected during the period July 2007 to December 2012. Included in the study were all children who fulfilled the following criteria: age less than 16 years; presenting at the University of Zürich Children's Hospital during the study time period and the child's illness is being travel-related, in the opinion of the consulting physician. Data were obtained from the patients' charts and entered into the standardized anonymous form of the GeoSentinel database.[6] We assessed the following variables: demographic information (sex, age, clinic visit date, country of birth, country of citizenship and country of current residence), travel history during the previous 5 years taking into account the incubation period of the presenting illness, country of exposure, reason for travel related to current illness (eg, tourism, VFR, immigration and medical tourism), inpatient or outpatient status, main presenting signs and symptoms and physician-assigned diagnoses. The diagnoses assigned by the ER physicians were chosen from a list of >500[6] possible diagnoses by the study team or allocated to an appropriate syndromic group when no specific pathogen was identified.

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From the *WHO Collaborating Centre for Travellers' Heath, Epidemiology, Biostatistics and Prevention Institute, University of Zürich, Switzerland; †Division of Infectious Diseases and Hospital Epidemiology, ‡Children's Research Centre, University Children's Hospital Zürich, Zürich, Switzerland; §Center for Global Health and Development, ¶Department of Global Health, Boston University School of Public Health, Boston, Massachusetts; ‖Section of Infectious Diseases, Department of Medicine, Boston Medical Center, Boston, Massachusetts; and **Division of Infectious Diseases and Hospital Epidemiology, University Hospital Zurich, University of Zurich, Zurich, Switzerland.

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Address for correspondence: Patricia Schlagenhauf, PhD, WHO Collaborating Centre for Travellers' Heath, Epidemiology, Biostatistics and Prevention Institute, University of Zürich, Zürich, Switzerland. E-mail: pat@ifspm.uzh.ch.

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Definitions

"Immigration travel" was assigned if the only relevant international travel was the primary immigration journey into Switzerland. A VFR was defined as first or second generation immigrant, VFR in the country of the family's origin. Tourism denotes crossing an international border and traveling for holiday abroad without visiting first or second generation family members. Medical tourism describes travel where entry into a country, which is not the patient's current country of residence, is for the primary purpose of seeking elective or emergency medical care for a condition existing in the country of residence.[6] Countries of exposure were assigned to a region of exposure according to a slightly modified version of the United Nations geoscheme.[7]

Statistics

Excel was used for the statistical analysis. *P* values were calculated with excel using the χ^2 test. A *P* value of less than 0.05 was considered significant.

Ethics Statement

GeoSentinel surveillance data are classified as public health surveillance of anonymous data by the National Centre for Emerging and Zoonotic Infectious Disease at the US Centers for Disease Control and Prevention.

RESULTS

During the period July 2007 to December 2012, a total of 179,100 pediatric patients attended the ER of University of Zurich Children's Hospital; 88.4% were treated as outpatients and 11.6% as inpatients. A total of 801 children (0.45% of all the ER consultations) were tagged with suspected travel-related illness; of these, 57.4% were male. The age range was 0–16 years (average age = 4.4 years) (median age = 3 years). Four hundred and twenty-eight (53.4%) of all the patients with travel-related conditions were VFR travelers, 348 (43.4%) tourists, 19 (2.4%) immigrants and 6 (0.7%) of the patients had another purpose of travel [eg, business (with parents), student and medical tourism]. The median travel duration was 19.5 days (range, 1–63 days). Main regions of exposure were Southern Europe, 275 (34.3%); Western Asia, 79 (9.9%); South/Central America, 67 (8.4%); Southern Asia, 64 (8.0%); Northern Africa, 50 (6.2%); Sub-Saharan Africa, 48 (6.0%); Western Europe, 35 (4.4%) and South-Eastern Asia, 35 (4.4%). In 89 (11.1%) patients, the region of exposure was not ascertainable (see Table, Supplemental Digital Content 1, http://links.lww.com/INF/C246). For both inpatients and outpatients, gastrointestinal symptoms and fever were the most frequently presenting symptoms as shown in Table 1. The most frequent syndromes were "acute diarrhea," 317 (32.5%); "respiratory," 264 (27.1%); "febrile/systemic illness," 91 (9.4%) and "dermatologic illness," 79 (8.1%) (Fig. 1). The diagnoses in inpatients and outpatients are shown in Table 2.

Comparison of Inpatients Versus Outpatients

Our analysis included 83 (10.4%) inpatients and 718 (89.6%) outpatients. The number of males within the inpatients was significantly higher compared with an expected rate of 50% (*P* = 0.0133). When comparing inpatients and outpatients, the male proportion was higher within the inpatients (66.3% vs. 56.4%) (see Table, Supplemental Digital Content 1, http://links.lww.com/INF/C246). Age distribution was similar in inpatients and outpatients. However, half of the patients admitted to the hospital and outpatients (50.6% inpatients and 48.1% outpatients) were younger than 2 years of age indicating an overrepresentation of this age group among ill returning children. With respect to the region of exposure and treatment as an inpatient or outpatient, our results show a nonsignificant trend in that Southern Europe was the most frequent region of exposure for both groups, with a lower percentage for inpatients (28.9%) than for outpatients (35.0%). However, for children travelling to Southern Asia, there was a significant association with hospitalization (*P* = 0.0015) as shown in Table 1. Forty-four and 33 children returning from VFR and tourist travel, respectively, required hospitalization; the proportion of inpatients among VFR travelers was 10.3% (44 of 428) and thus only slightly higher than for tourist travel (33 of 348; 9.5%). The number of immigrants in this series was low, but nevertheless, 4 of 19 (21%) immigrant children needed to be admitted to the hospital, and severe disease was overrepresented among them.

Gastrointestinal symptoms and fever were the most frequent symptoms, for both inpatients and outpatients. Fever was more common in inpatients (75.9% vs. 51.7%, *P* = 0.003). Inpatients presented more often with neurologic symptoms or lymphadenopathy (*P* < 0.0001) (Table 1). Acute diarrhea was the most common diagnosis among both inpatient and outpatient groups but more frequent in outpatients than in inpatients (34.3% vs. 21.6%, *P* = 0.0151). Also, outpatients more often presented with respiratory infections (25.1% vs. 14.4%, *P* = 0.0163). Inpatients were more likely to suffer of *Salmonella typhi* or *Salmonella paratyphi* (inpatients 3.6 % vs. outpatients 0.1%, *P* ≤ 0.0001), pyogenic abscess (inpatients 3.6% vs. outpatient 0.1 %, *P* value ≤ 0.0001)

TABLE 1. Primary Presenting Symptoms and Signs That Led to Clinic Visits (Percentage Expressed as Number of Symptoms Per Total Patients in Each Group)

Primary symptom(s)	Inpatients, n (%)	Outpatients, n (%)	*P* Value
Gastrointestinal	50 (60.2)	403 (56.1)	0.629
Fever	63 (75.9)	371 (51.7)	0.003
Respiratory	24 (28.9)	181 (25.2)	0.5112
Head, ear, eyes, nose and throat	16 (19.3)	156 (21.7)	0.6338
Skin	8 (9.6)	98 (13.6)	0.3188
Neurologic	10 (12.0)	18 (2.5)	<0.0001
Genitourinary	4 (4.8)	12 (1.7)	0.0465
Musculoskeletal	5 (6.0)	10 (1.4)	0.0027
Lymphatic	7 (8.4)	6 (0.8)	<0.0001
Fatigue	3 (3.6)	7 (1.0)	0.0279
Abnormal lab test	5 (6.0)	3 (0.2)	<0.0001
Other	3 (3.6)	0 (0)	<0.0001
Cardiac	1 (1.2)	0 (0)	0.0005
Total count	199	1265	
Mean count of symptoms/patient	2.4	1.8	

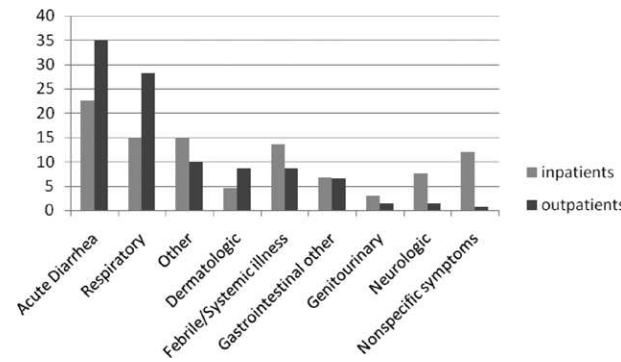

FIGURE 1. Inpatients versus outpatients proportion of the different syndrome groups.

TABLE 2. Summary Diagnosis and Syndrome Groups (Inpatients Compared with Outpatients)

Summary Diagnosis and Syndrome Groups	Inpatients, n (%)	Outpatients, n (%)	*P* Value
Acute diarrhea	30 (21.6)	286 (34.3)	0.0151
Chronic diarrhea	0 (0)	11 (1.3)	0.1689
Appendicitis	4 (2.9)	0 (0)	<0.0001
Viral hepatitis, acute	1 (0.7)	3 (0.4)	0.5331
Leishmania, visceral	1 (0.7)	0 (0)	0.013
Salmonella typhi and *Salmonella paratyphi*	5 (3.6)	1 (0.1)	<0.0001
Febrile illness unspecified	3 (2.2)	31 (3.7)	0.3631
Dengue, uncomplicated	0 (0)	2 (0.2)	0.5575
Malaria (all species)	2 (1.4)	2 (0.2)	0.0384
Lyme disease—early disease	0 (0)	1 (0.1)	0.6783
Lyme disease—late disease	0 (0)	3 (0.4)	0.4725
Mycobacterium tuberculosis	2 (1.4)	1 (0.1)	0.0086
Respiratory infection, acute	20 (14.4)	209 (25.1)	0.0163
Viral syndrome	0 (0)	20 (2.4)	0.0705
Seizure disorder	5 (3.6)	3 (0.4)	<0.0001
Meningitis	1 (0.7)	1 (0.1)	0.1433
Encephalitis, viral	1 (0.7)	0 (0)	0.013
Neurocysticercosis	1 (0.7)	0 (0)	0.013
Ophthalmologic disorder	0 (0)	9 (1.1)	0.2134
Dermatologic disorder	7 (5.0)	72 (8.6)	0.2106
Dehydration	12 (8.6)	5 (0.6)	<0.0001
Anemia	3 (2.2)	0 (0)	<0.0001
Abscess, pyogenic, not skin, not tonsillar, not liver, not dental	5 (3.6)	1 (0.1)	<0.0001
Adverse events to medication or vaccine	1 (0.7)	1 (0.1)	0.1433
Other	35 (25.2%)	172 (20.6)	
Total	139	834	

TABLE 3. Diagnosis of Special Interest with Region of Exposure, Inpatient or Outpatient Status and Travel Reason

Diagnosis	Travel Destination	Patient Type	Travel Reason
Dengue, uncomplicated	Cuba	O	VFR
	Thailand	O	Tourism
Encephalitis, viral	Serbia	I	VFR
Hepatitis A, acute	Serbia	O	VFR
	Kosovo	I	VFR
	Côte d'Ivoire	O	VFR
Leishmania, visceral	Portugal	I	VFR
Lyme disease, acute or early disease	Netherland	O	Tourism
Lyme disease, late or chronic	United States	O	Tourism
	United Kingdom	O	Tourism
	Australia	O	VFR
Malaria, *Plasmodium falciparum*	Ghana	I	VFR
	Nigeria	O	VFR
	Ghana	I	Immigration
Malaria, *Plasmodium vivax*	Ethiopia	O	Immigration
Mycobacterium tuberculosis	Turkey	O	VFR
	Kosovo	I	VFR
	Tibet	I	Immigration
Neurocysticercosis	South-eastern Asia	I	Tourism
Salmonella typhi and *Salmonella paratyphi*	Bangladesh	I	VFR
	Iraq	I	VFR
	Turkey	I	VFR
	Turkey	I	Tourism
	Italy	I	Tourism
	India	O	Tourism

O indicates outpatient; I, inpatient.

or malaria (inpatients 1.4 % vs. outpatients 0.2%, $P = 0.0384$). A neurologic syndrome (eg, seizure disorder: inpatients 3.6% vs. outpatients 0.4%, $P \leq 0.0001$) was more often diagnosed among inpatients. Finally, inpatients more often suffered from nonspecific findings such as dehydration (8.5% vs. 0.6%, $P \leq 0.0001$) (Table 2). Table 3 shows some diagnoses that are of special interest, that is, rare or exotic infections. Of the total 25 diagnoses of special interest, there were 8 tourists, 14 VFRs and 3 immigrants. In total, there were only 4 malaria cases (3 *Plasmodium falciparum* and 1 *Plasmodium vivax*), all from sub-Saharan Africa. There were 3 tuberculosis cases, 1 from Turkey, 1 from Kosovo and 1 from Tibet. The neurocysticercosis case was an 11-year-old boy traveling with his parents as a tourist in South-eastern Asia.

DISCUSSION

In this study, ill-returned children had mainly acute diarrhea or respiratory infections. This was also shown in an earlier study of travel-associated illness in children.[8] Some 10.4% of the children presenting with a travel-related disease were hospitalized. When comparing inpatients and outpatients, the following variables were significantly associated with hospitalization: children returning from Southern Asia, children with febrile/systemic illness (such as malaria, typhoid fever), neurologic diseases and children with nonspecific findings such as dehydration. There was no correlation between VFR travel and hospitalization.

It has been shown that travel destination influences the risk of acquiring certain illnesses for children.[5,9] Systemic/febrile illness occurs most often in children traveling to Sub-Saharan Africa, diarrhea is associated with travel to the Middle East/Southern Asia and North Africa, dermatological illness occurs frequently after exposure in Latin America and respiratory infections are associated with travel in Europe or North Africa.[5] In our study population, Southern Europe was the most popular travel destination (34.3%) often visited by VFRs and by tourists. Immigrant populations from Serbia and Montenegro; Macedonia; Croatia; Bosnia and Herzegovina; Spain; Portugal and Italy comprise approximately half of the current foreign population in Switzerland.[10] This results in a significant proportion of VFR travel to these countries. Tourist travel was mainly to Italy, Greece, Spain and Portugal.[4]

Children traveling to Southern Asia had a significant risk of hospitalization. Southern Asia including India has one of the highest global incidences of infections such as typhoid fever. Global studies of adult travelers have shown that VFR travelers and immigrants are at higher risk to acquire certain travel-related disease compared with traditional travelers.[11–15] Immigrants and VFR travelers are more likely to have a diagnosis such as malaria, typhoid fever, hepatitis A, hepatitis B and tuberculosis compared with tourist travelers.[13,15] Our study confirms these findings in children. All hepatitis A, malaria and tuberculosis cases were diagnosed in VFR travelers and immigrants. Typhoid fever was diagnosed in 3 VFR and 3 tourist travelers.

Diarrhea was the most common travel-related diagnosis in our study. The same is true for the study of American pediatric travelers.[9] In adults, travelers' diarrhea is usually a mild albeit difficult to prevent, using the current strategies.[15] Young children have a higher risk of having severe illness and are more susceptible to the effects of gastrointestinal fluid losses.[16] This may result in hypovolemia requiring intravenous fluids and/or hospitalization. In our study, a significant proportion of children suffering from diarrhea experienced dehydration and, therefore, had to be hospitalized. Pretravel travel-health advice can play an important role in the prevention of dehydration caused by travelers' diarrhea. Parents traveling with children should be informed about common food and water precautions.[16]

Convenient oral rehydration sachets should be an essential part of a first-aid kit when traveling with children.[17,18] Loperamide is recommended for children older than 2 years in the US. In Switzerland, it is recommended only for children older than 6 years.

With regard to vaccine preventable infection, hepatitis A is usually mild in children, but this pretravel vaccination should be recommended for VFR children who will not be immune. Our study showed 3 cases of hepatitis A, all in VFR travelers. Furthermore, the typhoid fever vaccine should also be recommended for children traveling to Asia, but the live oral Ty21a vaccine is only licensed for use in children older than 6 years. The polysaccharide Vi vaccine, not registered in Switzerland, but available in other countries, is licensed for use in children older than 2 years.

Children have been shown to be risk of dermatological problems during travel.[19] Our study confirmed that pediatric travelers can present with a range of dermatological conditions including infected arthropod bites, scabies and cutaneous larva migrans (data not shown), but these are treated mainly in an outpatient setting.

Our study had some limitations: patients were included in the study if the ER physician marked the diagnosis as "travel-related" in the patient's file. We have to assume that some cases were missed. Furthermore, we only analyzed the data of children who visited University of Zurich's children hospital, and this does not represent the whole population of Zurich. We have no data on the number of travelers returning healthy or the proportion of children who were treated abroad. Thus, this analysis does not allow for the calculation of risk or incidence rates because of missing denominator data.

Children present with a broad spectrum of travel-related disease. Travel history is essential. Physicians should be knowledgeable about the probabilities of the occurrence of travel-related pathogens according to geographic areas[20,21] and recommend diagnostic methods and empiric therapies accordingly. The data are also important for pretravel health advisors to allow them to tailor advice and to focus on the prevention of frequently occurring disorders, such as travelers' diarrhea, and less frequent but severe infections, such as malaria, hepatitis A and typhoid fever. In conclusion, this study shows that it is not always an exotic diagnosis such as dengue or tuberculosis, which may lead to hospitalization of a child returning from international travel. Often, in a child, it is travelers' diarrhea that may require hospitalization, and this can be contracted at all travel destinations.

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